friction-fit or jammed into the machined holes on the top surface of the manifold. This may create trapped air dead volumes in the manifold.

[0064] FIG. **2** shows a Fluidic Manifold system with a two piece design, including an aluminum bezel. This can reduce temperature-induced warping of manifolds, such as polycarbonate (PC) manifolds. The small PC fluidic manifold, housed in the aluminum bezel, can be modified with large diameter holes that function as reagent wells (without pipette tips). These enlarged holes can permit pipetting of reagents directly into chip wells. This feature can eliminate air dead volumes in reagent wells, and greatly reduces the number of priming cycles required, compared with the original design. Holes labeled Out**1**/Out**2** can be interfaced with a pipette tip. FIG. **3** is a photograph of a complete system, including TEC-Tip Manifold with four TEC stacks.

[0065] As shown in FIG. **4**, the TEC-Tip Manifold can comprise an aluminum manifold and multiple "TEC stacks." As shown in FIG. **4**A, a Peltier TEC can be attached to heat sink and to manifold with heat-conductive PSA. A Fan can be glued to heat sink fins. As shown in FIG. **4**B, Four series connected TECs can be connected to H-Bridge. H-Bridge can rout power to TECs in response to signals from FTC100 controller. The aluminum manifold can have four holes drilled in its center to house the four pipette tips connected to chip Out**1** and Out**2** wells. As described above, the tips can function as reservoirs for mixing and incubation steps. The purpose of the TEC-Tip Manifold can be to control the temperature of incubations over a range of 16C to 65C. Temperature can be controlled through the action of "TEC stacks" attached to the aluminum manifold, as shown in FIG. **3** and FIG. **13**. As shown in FIG. **4**A, each stack can comprise three main parts: Peltier TEC, heat sink, and fan. As illustrated in FIG. **4**B, the TEC stacks can either heat or cool the manifold in response to current supplied by the H-Bridge. The H-Bridge can be controlled by two signals (level and direction) from the FTC100 controller, which implements a PID control system. The FTC100 can compute values for these signals based on the temperature of the manifold, as measured by a thermocouple implanted in it, user programmed set point, and PID parameters: P (proportional), I (integral), and D (differential). PID parameters can be set automatically using the Autotune function of the FTC100. The minimum operating voltage of the H-Bridge may be 7 volts, which may require a series connection of the four TECs, each rated at 3 volts maximum. The system can be typically operated at 8 volts for cooling and heating to 40C. Higher voltages (up to 12 volts) could be used for heating to 65C and above. Fans can be driven continuously by a separate 5 volt power supply.

[0066] The systems, devices, and methods described herein can be pipette-free. Reservoirs can be designed to be included within the cartridge, or any other component, such that pipettes are not needed. An example of such a system is shown in FIG. **5** and FIG. **6**.

[0067] FIG. **5** shows a system comprising a base, e.g., an aluminum manifold, that supports other structures and that can function as a heat sink. Thermal regulators, e.g., thermoelectric couplers, are mounted on the base and are in thermal contact with the base, e.g., to allow heat exchange.

[0068] A pneumatic manifold comprising vias, e.g., a pneumatic floater, also is mounted on the base. It can be biased, e.g., with springs, so that it can make a pressurized seal with a microfluidic chip. Pneumatic inserts can engage vias in the pneumatic manifold on the side that does not engage the microfluidic chip. The pneumatic inserts communicate with pneumatic lines that supply pressure (positive or negative) to the pneumatic layer of the microfluidic chip.

[0069] A microfluidic device is mounted on the base. The microfluidic device includes a microfluidic chip and a cartridge, e.g. a reservoir. The microfluidic chip comprises a fluidic layer, a pneumatic layer and an elastic layer sandwiched between them. The fluidic layer comprises microfluidic channels that open on an outside surface of the fluidic layer and an inside surface of the fluidic layer. The pneumatic layer also comprises pneumatic channels that open on an outside surface of the pneumatic layer and an inside surface of the pneumatic layer. Where fluidic channels and pneumatic channels open onto the elastic layer opposite each other, diaphragm valves and other micromachines can be formed. Applying positive or negative pressure on a port in a pneumatic channel deflects the elastic layer and opens or closes valves in the fluidic channels to allow liquid to pass, or to pump liquid through a channel. This can occur when the chip is engaged with the pneumatic manifold so that the vias in the manifold are in pneumatic communication with ports in the pneumatic channels. The actuant can be air, but also can be a hydrolic fluid. The microfluidic device also comprises a cartridge.

[0070] The cartridge comprises compartments and wells that open on two surfaces of the reservoir. One side of the cartridge is engaged with the microfluidic chip. Ports in both parts are aligned with one another so as to be in fluidic communication. In this way, the chip can direct fluid in a various wells or compartments in the cartridge to other wells or compartments in the cartridge. The wells and compartments in the cartridge can have volumes in the mesofluidic or macrofluidic scale, that is between a microliter and tens of microliters, hundreds of microliters, milliliters, tens of milliliters or more. For example, the reservoir can comprise serpentine channels that can comprise reaction mixtures placed there by pumping liquid from wells in the cartridge that mate with ports on the chip, through pumps or valves in the microfluidic chip, out of the chip and into the compartments on the reservoir. For reaction mixtures that must be maintained at temperature, or undergo thermal cycling, the compartments holding these mixtures, e.g., the serpentine channels, can be positioned such that when the microfluidic device is loaded on the base, the compartments are in thermal contact with the heat controlling devices, e.g., the thermoelectric couplers.

[0071] The microfluidic device can be held in place by, for example, screws, clamps, etc. When pressed against the base, the microfluidic chip also engages the pneumatic manifold. When the pneumatic manifold is biased, a tight fit between the pneumatic manifold and the microfluidic chip, as well as between the reservoir and the thermal controllers, are maintained without the need for exact tolerances in loading the pneumatic manifold on the base.

[0072] As shown in FIG. **5** and FIG. **6**, serpentine channels can be used as reaction chambers. The serpentine channels can be interfaced with temperature controlling devices, such as thermoelectric coolers. The temperature controlling device can be used to control the temperature of a component. It can utilize Peltier devices or heated or cooled liquids, gases, or other materials. The temperature controlling devices can be housed in a base, which may include a pneumatic floater, pneumatic inserts, and springs, described herein.

[0073] As shown in FIG. **5**, the Fluidic Manifold can comprise two parts: Reservoir and Reservoir Bottom. The Reser-